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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/840,085	04/24/2001	Alanna Schepartz Shrader	Y0087.70010US00	2186

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EXAMINER

ALLEN, MARIANNE P

ART UNIT	PAPER NUMBER
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1647

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/28/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 09/840,085	Applicant(s) SHRADER ET AL.	
	Examiner Marianne P. Allen	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12/4/06, 1/26/07, 2/20/07.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,14-22,24,25 and 28-31 is/are pending in the application.
- 4a) Of the above claim(s) 14-18 and 20-22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,19,24,25 and 28-31 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1,14-22,24 and 28-31 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The amendments filed 12/4/06, 1/26/07, and 2/20/07 have been entered. Claims 2-13, 23, and 26-27 have been cancelled. Claims 28-31 have been newly added. Claims 14-18 and 20-22 remain withdrawn as being drawn to a nonelected invention. Claims 1, 19, 24-25, 28-29, and 30-31 are under consideration by the examiner.

Applicant's arguments accompanying the 12/4/06, 1/26/07, and 2/20/07 responses have been fully considered but they are not persuasive.

The rejection of claims 1-5, 12-13, 23, 24, and 25 under 35 U.S.C. 102(b) as being anticipated by Chittenden et al. (U.S. Patent No. 5,656,725) is withdrawn in view of the amendments to the claims.

The rejection of claims 1-5, 12-13, and 23-25 under 35 U.S.C. 103(a) as being unpatentable over Zondlo et al. (J. Am. Chem. Soc., 121:6938-939, 1999) in view of Sattler et al. (Science, 275:983-986, 1997) is withdrawn in view of the amendments to the claims.

Claim Objections

Claims 30-31 are objected to because of the following informalities: These claims recite sequences without referring to the appropriate sequence identifiers.

It is not obvious whether these sequences are present in the sequence listing. If they are not, the application is not in compliance with 37 CFR 1.821-1.825.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 1, 24-25, and 28-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which

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was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 1 as amended is directed to an avian pancreatic polypeptide of SEQ ID NO: 6 modified by substitution of at least one amino acid residue wherein the modified avian pancreatic polypeptide comprises an amino acid sequence selected from SEQ ID NOS: 23, 24, 25, 26, 27, 28, or 29.

While isolated polypeptides comprising the amino acid sequence of SEQ ID NOS: 23, 24, 25, 26, 27, 28, or 29 are described and enabled, claim 1 as presently written is not limited to each of these polypeptides in the alternative. SEQ ID NO: 6 is a 36 amino acid sequence. Each of SEQ ID NOS: 23, 24, 26, 27, 28, and 29 is a 15 amino acid sequence. SEQ ID NO: 25 is a 14 amino acid sequence. In view of the disclosure in the specification (particularly Figure 4), only three positions are considered to correspond to the base avian polypeptide. (See amino acid positions 1, 5, 8 of SEQ ID NO: 30 in Figure 4 corresponding to amino acid positions of 20, 23, 27 of SEQ ID NO: 6. Each of these amino acids is retained in SEQ ID NOS: 23, 24, 25, 26, 27, 28, and 29.) As such, a fair reading of the claim must mean that SEQ ID NOS: 23, 24, 25, 26, 27, 28, or 29 may be present anywhere within SEQ ID NO: 6 and additionally permitting more substitutions in SEQ ID NO: 6 outside of this range. For example, claim 1 is considered to include SEQ ID NO: 6 where SEQ ID NO: 23 replaces amino acid positions 1-15 of SEQ ID NO: 6. Any or all of positions 16-36 of SEQ ID NO: 6 may also be substituted. Claim 1 is also considered to include SEQ ID NO: 6 where SEQ ID NO: 25 replaces amino acid positions 23-36 of SEQ ID NO: 6. Any or all of positions 1-22 may also be substituted. These polypeptides

and other polypeptides within the scope of claims are not contemplated by the specification as originally filed.

New claim 28 explicitly recites that portions of SEQ ID NO: 6 are replaced by SEQ ID NOS: 23, 24, 25, 26, 27, 28, or 29. There is no apparent basis in the specification for replacing any portion of SEQ ID NO: 6 with the recited SEQ ID NOS. for the reasons set forth above.

Applicant points to Figure 6; page 8, lines 4-7, and SEQ ID NO: 25 for basis for new claim 30. This is not agreed with. The general model in Figure 6 does not speak to designing proteins for Bcl2 binding. The claim is not limited to either of the sequences depicted below the figure. Neither Figure 6 nor page 8, lines 4-7, refer to retaining particular amino acids of SEQ ID NO: 25 as a preferred embodiment as argued by applicant in the response. The polypeptides embraced by claim 30 are not contemplated in general or in specific by the sections pointed to.

Likewise, applicant's stated basis for claim 31 is not agreed with. Figure 4 does not discuss or contemplate inclusion of a hydrophobic core from Figure 6. The consensus sequence discussed by applicant on page 8 of the response filed 2/20/07 is not present in either of these figures. At best, SEQ ID NO: 30 (corresponding to the top line BakLIB) is disclosed and claim 31 is not limited to this sequence. This claim is not limited to the sequence set forth on the bottom of page 8 of the 2/20/07 response. It is noted that amino acid position 36 of SEQ ID NO: 6 corresponds to Tyr and not amino acid position 35. Amino acid position of SEQ ID NO: 6 is His.

Claims 1, 19, 24-25, and 28-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NOS: 23-29 does not reasonably provide enablement for avian pancreatic polypeptides with the stated substitutions and properties. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The disclosure makes clear that the miniature proteins must retain a particular structure in order for binding to the intended target to occur. This structure is achieved by retaining particular portions of SEQ ID NO: 6 and substituting specific amino acids at specific positions within amino acids 20-34 of SEQ ID NO: 6. The claims embrace modifying positions that result in miniature proteins that would not be expected to bind. Figure 4 shows how slight changes to the sequence greatly effects binding. The specification does not tell how to use miniature proteins that do not bind to the intended target.

With respect to claim 19, SEQ ID NO: 23 is a 15 amino acid peptide. Removing three amino acids as a group or individually would appear to result in a non-functional miniature protein. (See part (b).) Even though the claim requires that the polypeptide binds to a Bcl-2 protein, the specification does not provide guidance on which fragments would provide this result. Note that the at least twelve amino acids are not required to be contiguous and could embrace SEQ ID NO: 23 where amino acids 1, 8, and 11 are missing. These positions are disclosed as forming the needed alpha helix. Even with respect to the natural and conservative amino acid substitutions, substituting at most positions would be expected to make the peptide non-functional.

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The specification does not provide guidance as to those polypeptides encompassed by claims 30-31 that will bind to Bcl2 protein in addition to SEQ ID NOS: 23-29. Given the breadth of the claims, the structural constraints for binding Bcl2 disclosed by the specification, and the sequence similarity of SEQ ID NOS: 23-29, the claims are considered to embrace inoperative embodiments and/or lack guidance as to additional embodiments expected to bind. Note that the positions recited in the claims (e.g. 17, 20, 27, 30) are not clearly with respect to SEQ ID NO: 6 or any other sequence. Note that the 13 amino acid sequence recited in claims 30 and 31 is not required to be located in any particular position within the polypeptide. That is, this sequence could occur at the C-terminal end of the peptide rather than the N-terminal end of the peptide. Any and all positions of SEQ ID NO: 6 are permitted to be modified by substitution.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 19 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The preamble of claim 19 is directed to a modified avian pancreatic polypeptide. SEQ ID NO: 23 is a 15 amino acid sequence where only three amino acids have been identified by the specification as corresponding to an avian pancreatic polypeptide (compare SEQ ID NO: 23 with amino acids 20-34 of SEQ ID NO: 6). Given the degree of substitution and the fact that SEQ ID NO: 23 bears little resemblance to any naturally occurring peptide from any tissue or species, the language "avian pancreatic polypeptide" is misleading or confusing. It is unclear if the intent is

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to require unspecified structural features. That is, the specification does not make disclose when a polypeptide is considered an avian pancreatic polypeptide and when it can no longer be classified as such due to modification. It is suggested that the language "avian pancreatic" be removed from the claim.

Parts (c) and (d) require at least 90% identity to SEQ ID NO: 23 with one or more substitutions. It is unclear what a "naturally occurring amino acid substitution" would be as SEQ ID NO: 23 is not a naturally occurring sequence. Some positions are attributed to Bak and some are attributed to aPP. It is a synthetic polypeptide. The claim is further confusing because having "at least 90%" of a fifteen amino acid peptide would permit one substitution but the claim recites "one or more." Part (d) requires at least 95% identity to SEQ ID NO: 23. This would permit $\frac{3}{4}$ (i.e. not even one) amino acid substitution. Clarification is requested.

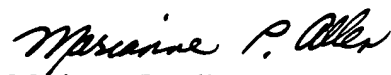
Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen whose telephone number is 571-272-0712. The examiner can normally be reached on Monday-Friday, 5:30 am - 2:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Marianne P. Allen
Primary Examiner
Art Unit 1647

2/22/07

mpa